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Remarks

Reconsideration of this Application is respectfully requested.

Upon entry of the foregoing amendment, claims 6 and 19 have been cancelled without prejudice or disclaimer, claims 1, 7-8, 18, and 20-21 are pending in the application, with claims 1 and 18 being the independent claims. Claims 1, 7-8, 18, and 20-21 have been amended taking the Examiner's comments into consideration. These changes are believed to introduce no new matter, and their entry is respectfully requested.

Support for the amended claims may be found throughout the specification. In particular, support for claims 1 and 18 may be found, *inter alia*, at page 4, lines 21-25, Example 2 and Table A. Support for claims 7 and 18-21 may be found, *inter alia*, at page 8, line 24; at page 10, line 24 and in Example 2.

Based on the above amendment and the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding rejections and that they be withdrawn.

Document AT3 on PTO-1449 Form

In the Amendment and Reply Under 37 C.F.R. § 1.116, filed on December 20, 2001, Applicants have requested the Examiner to consider Document AT3 which was filed in an Information Disclosure Statement on July 21, 2000. For the convenience of the Examiner, Applicants submit herewith a copy of document AT3 which was not considered by the Examiner.

Applicants respectfully request that the Examiner review this document and forward a PTO-892 form to acknowledge consideration in the next communication.

Objection to Title

In the Office Action at page 2, the Examiner has objected to the title as allegedly being non-descriptive. Solely to advance prosecution and not in acquiescence to the Examiner's rejection, Applicants have amended the title as suggested by the Examiner. Accordingly, reconsideration and withdrawal are respectfully requested.

Objection to Claims 1 and 6

In the Office Action at page 2, the Examiner has objected to claims 1 and 6 for lack of clear recitation of the full term for *pgi*. Solely to advance prosecution and not in acquiescence to the Examiner's rejection, Applicants have amended claim 1 as suggested by the Examiner. Claim 6 has been cancelled and thus rending this objection moot as to claim 6. Accordingly, reconsideration and withdrawal are respectfully requested.

Objection to Claims 7 and 20

In the Office Action at page 2, the Examiner has objected to claims 7 and 20 as allegedly being of improper dependent form. Applicants respectfully disagree with the Examiner's conclusion. Claims 7 and 20 further specify the type of disrupted *pgi* gene in the altered *Corynebacterium* cell and thus are proper dependent claims. These claims limit the disrupted *pgi* gene to a mutant *pgi* gene. As stated in the specification, reference to a

disrupted *pgi* gene is a general characteristic and a mutant *pgi* gene is more specific. Accordingly, reconsideration and withdrawal are respectfully requested.

Rejection Under 35 U.S.C. § 112, Second Paragraph

In the Office Action at page 3, claims 8 and 21 are rejected under 35 U.S.C. § 112, second paragraph for alleged indefiniteness for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. Applicants respectfully traverse this rejection.

The Examiner stated that:

> [c]laims 8 and 21 are incomplete as carrying out steps (a) and (b) do not necessarily result in disruption of a pgi gene. One of skill in the art would recognize that by inserting an internal region of a gene by homologous recombination would recreate the original gene. It is noted that the specification discloses at lines 4 and 5 of page 30 that the vector into which the internal fragment was cloned is a suicide vector. It is suggested that applicants clarify the meaning of the claims.

Office Action at 3. Applicants respectfully disagree with the Examiner's assertion that claims 8 and 21 are incomplete. However, solely to advance prosecution and not in acquiescence to the Examiner's rejection, claims 8 and 21 are amended to recite "suicide vector." Accordingly, reconsideration and withdrawal are respectfully requested.

Furthermore, the Examiner has rejected claims 8 and 21 as allegedly having insufficient antecedent basis. Applicants respectfully disagree with the Examiner's conclusion. However, solely to advance prosecution and not in acquiescence to the Examiner's rejection, Applicants have amended claims 8 and 21 to recite "into a vector." Accordingly, reconsideration and withdrawal are respectfully requested.

Rejection under 35 U.S.C. § 112, First Paragraph

In the Office Action at page 4, claims 1, 6-8, and 18-21 are rejected under 35 U.S.C. § 112, first paragraph for alleged non-enablement. Applicants respectfully traverse this rejection.

The Examiner stated that:

> the specification . . . does not reasonably provide enablement for method of producing L-lysine, L-threonine, or L-isoleucine by culturing an altered C. glutamicum cell having a disrupted pgi gene with yields greater than about 25% relative to a C. glutamicum cell having a non-disrupted pgi gene or a method of producing L-lysine, L-threonine, or L-isoleucine by culturing an altered C. glutamicum cell having a decreased amount of 6-phosphoglucose isomerase enzyme activity and a disrupted pgi gene with yields greater than about 25% relative to a C. glutamicum cell having a non-disrupted pgi gene.

Office Action at page 4. Applicants respectfully disagree with the Examiner' s statement. However, solely to advance prosecution and not in acquiescence to the Examiner's rejection, Applicants have amended claims 1 and 18 to recite "from about 1% to about 25."

Accordingly, reconsideration and withdrawal are respectfully requested.

Conclusion

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite

prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.

Michele A. Cimbala
Attorney for Applicants
Registration No. 33,851

Date: Feb. 19, 2003

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(202) 371-2600

Version with markings to show changes made

In the Title:

Please substitute the following Title of the Invention for the pending Title of the Invention:

Method for Producing L-Amino Acids using a *Corynebacterium glutamicum* with a Disrupted pgi Gene

In the Claims:

(a) Claims 6 and 19 are cancelled.

(b) Claims 1, 7, 8, 18 and 20-21 are amended as follows:

1. (Thrice Amended) A method of producing an amino acid selected from the group consisting of L-lysine, L-threonine and L-isoleucine comprising:

culturing an altered *Corynebacterium glutamicum* cell, wherein said *Corynebacterium glutamicum* cell has a disrupted [*pgi*] phosphoglucose isomerase (*pgi*) gene, wherein yields of an amino acid selected from the group consisting of L-lysine, L-threonine and L-isoleucine from said altered *Corynebacterium glutamicum* cell having a disrupted *pgi* gene are from about 1% to about 25% greater than yields from a *Corynebacterium glutamicum* cell having a non-disrupted *pgi* gene.

7. (Thrice Amended) The method of claim 1, wherein said [altered *Corynebacterium glutamicum* cell has a] disrupted *pgi* gene is a mutant phosphoglucose isomerase [*pgi*] gene.

8. (Thrice Amended) The method of claim 1, wherein said altered *Corynebacterium glutamicum* cell having a disrupted *pgi* gene is produced by

(a) subcloning an internal region of a *pgi* gene into a vector; and

(b) inserting said resulting vector from step (a) into a *Corynebacterium glutamicum* genome via homologous recombination.

18. (Twice Amended) A method of producing L-amino acids selected from the group consisting of L-lysine, L-threonine and L-isoleucine, comprising:

culturing an altered *Corynebacterium glutamicum* cell having a decreased amount of 6-phosphoglucose isomerase enzymatic activity as compared to an unaltered *Corynebacterium glutamicum* cell wherein said L-amino acid yields from said altered *Corynebacterium glutamicum* cell are from about 1% to about 25% greater than yields from an unaltered *Corynebacterium glutamicum* cell.

20. (Twice Amended) The method of claim 18, wherein said [altered *Corynebacterium glutamicum* cell has a] disrupted *pgi* gene is a mutant pgi gene.

21. (Thrice Amended) The method of claim 18, wherein said altered *Corynebacterium glutamicum* cell having a disrupted *pgi* gene is produced by

(a) subcloning an internal region of a *pgi* gene into a vector; and

(b) inserting said resulting vector from step (a) into a *Corynebacterium glutamicum* genome via homologous recombination.

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ID   G6PI_MYCTU     STANDARD;      PRT;   553 AA.
AC   P77895;
DT   15-JUL-1998 (Rel. 36, Created)
DT   15-JUL-1998 (Rel. 36, Last sequence update)
DT   30-MAY-2000 (Rel. 39, Last annotation update)
DE   GLUCOSE-6-PHOSPHATE ISOMERASE (GPI) (EC 5.3.1.9) (PHOSPHOGLUCOSE
DE   ISOMERASE) (PGI) (PHOSPHOHEXOSE ISOMERASE) (PHI).
GN   PGI OR RV0946C OR MTCY10D7.28.
OS   Mycobacterium tuberculosis.
OC   Bacteria; Firmicutes; Actinobacteria; Actinobacteridae;
OC   Actinomycetales; Corynebacterineae; Mycobacteriaceae; Mycobacterium.
RN   [1]
RP   SEQUENCE FROM N.A.
RC   STRAIN=H37RV;
RX   MEDLINE; 98295987.
RA   Cole S.T., Brosch R., Parkhill J., Garnier T., Churcher C., Harris D.,
RA   Gordon S.V., Eiglmeier K., Gas S., Barry C.E. III, Tekaia F.,
RA   Badcock K., Basham D., Brown D., Chillingworth T., Connor R.,
RA   Davies R., Devlin K., Feltwell T., Gentles S., Hamlin N., Holroyd S.,
RA   Hornsby T., Jagels K., Krogh A., McLean J., Moule S., Murphy L.,
RA   Oliver S., Osborne J., Quail M.A., Rajandream M.A., Rogers J.,
RA   Rutter S., Seeger K., Skelton S., Squares S., Sqares R., Sulston J.E.,
RA   Taylor K., Whitehead S., Barrell B.G.;
RT   "Deciphering the biology of Mycobacterium tuberculosis from the
RT   complete genome sequence.";
RL   Nature 393:537-544(1998).
CC   -!- CATALYTIC ACTIVITY: GLUCOSE 6-PHOSPHATE = FRUCTOSE 6-PHOSPHATE.
CC   -!- PATHWAY: INVOLVED IN GLYCOLYSIS AND IN GLUCONEOGENESIS.
CC   -!- SUBCELLULAR LOCATION: CYTOPLASMIC (BY SIMILARITY).
CC   -!- SIMILARITY: BELONGS TO THE GPI FAMILY.
CC   ----------------------------------------------------------------------
CC   This SWISS-PROT entry is copyright. It is produced through a collaboration
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CC   ----------------------------------------------------------------------
DR   EMBL; Z79700; CAB02004.1; -.
DR   TUBERCULIST; RV0946C; -.
DR   INTERPRO; IPR001672; -.
DR   PFAM; PF00342; PGI; 1.
DR   PRINTS; PR00662; G6PISOMERASE.
DR   PROSITE; PS00765; P_GLUCOSE_ISOMERASE_1; 1.
DR   PROSITE; PS00174; P_GLUCOSE_ISOMERASE_2; 1.
KW   Gluconeogenesis; Glycolysis; Isomerase.
SQ   SEQUENCE   553 AA;  59974 MW;  FB57DFFD16386AE4 CRC64;
     MTSAPIPDIT ATPAWDALRR HHDQIGNTHL RQFFADDPGR GRELTVSVGD LYIDYSKHRV
     TRETLALLID LARTAHLEER RDQMFAGVHI NTSEDRAVLH TALRLPRDAE LVVDGQDVVT
     DVHAVLDAMG AFTDRLRSGE WTGATGKRIS TVVNIGIGGS DLGPVMVYQA LRHYADAGIS
     ARFVSNVDPA DLIATLADLD PATTLFIVAS KTFSTLETLT NATAARRWLT DALGDAAVSR
     HFVAVSTNKR LVDDFGINTD NMFGFWDWVG GRYSVDSAIG LSLMTVIGRD AFADFLAGFH
     IIDRHFATAP LESNAPVLLG LIGLWYSNFF GAQSRTVLPY SNDLSRFPAY LQQLTMESNG
     KSTRADGSPV SADTGEIFWG EPGTNGQHAF YQLLHQGTRL VPADFIGFAQ PLDDLPTAEG
     TGSMHDLLMS NFFAQTQVLA FGKTAEEIAA DGTPAHVVAH KVMPGNRPST SILASRLTPS
     VLGQLIALYE HQVFTEGVVW GIDSFDQWGV ELGKTQAKAL LPVITGAGSP PPQSDSSTDG
     LVRRYRTERG RAG
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